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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,910	HUANG ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-16,18-20 and 22-33* is/are pending in the application.

4a) Of the above claim(s) *22-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-16,18-20,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/03&08/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-16, 18-20 and 22-33 are presented for examination.

Acknowledgement is made of the present application as a continuation of U.S. Patent Application No. 10/270,313, filed October 15, 2002 (now U.S. Patent No. 6,777,444), which is a continuation of U.S. Patent Application No. 09/851,425, filed May 9, 2001 (now U.S. Patent No. 6,608,108), which is a continuation-in-part of U.S. Patent Application No. 09/690,063, filed October 16, 2000 (now U.S. Patent No. 6,417,234), which is a continuation-in-part of U.S. Patent Application No. 09/418,594, filed October 15, 1999 (now U.S. Patent No. 6,214,874).

Applicant's Preliminary Amendment filed December 16, 2003 has been received and entered into the present application. Accordingly, the specification at pages 1, 7, 8, 13, 15, 17, 18, 19, 20-21, 26,29-30 and 36 has been amended, claims 1-8, 17 and 21 have been cancelled, claims 9-16 and 18-20 are amended and claims 22-33 are newly added.

Applicant's Information Disclosure Statements (IDS) filed December 16, 2003 (two pages) and August 21, 2006 (one page) have each been received and entered into the present application. As reflected by the attached, completed copy of form PTO/SB/08 (three pages total), the Examiner has considered the cited references except for the references designated as 17-19 and 21-24 on the IDS filed December 16, 2003. A reasonable search by the Examiner could not locate the references and, accordingly, they have not been considered.

Applicant's response filed August 21, 2006 to the requirement for restriction/election dated June 20, 2006 has also been received and entered into the present application.

Requirement for Restriction/Election

Applicant was required under 35 U.S.C. 121 to elect a single invention and a single disclosed species of compound of the formula recited in present claim 9 for prosecution on the merits to which the

claims will be restricted.

Applicant's election of the invention of Group I (claims 9-16, 18-20 and 32-33), directed to a method for treating a tumor comprising providing a composition comprising an effective amount of the compound recited in claim 9 and applying the composition to the tumor, and the species of M4N (tetra-O-methylnordihydroguairaretic acid; also known as meso-1,4-bis(3,4-dimethoxyphenyl)-(2R,3S)-dimethylbutane, see Figure 1 of the drawings) as the single disclosed species of compound as recited in present claim 9 in the reply filed August 21, 2006 is acknowledged. Insofar as Applicant has failed to particularly point out the supposed errors in the requirement for election, Applicant's election has been herein treated as an election **without traverse**. Please reference MPEP §818.03(a).

Therefore, for the reasons above and those made of record at pages 2-6 of the previous Office Action dated June 20, 2006, the restriction requirement remains proper and is made **FINAL**.

Claims 22-31 are **withdrawn** from consideration pursuant to 37 C.F.R. 1.142(b) as being directed to non-elected subject matter.

The claims corresponding to the elected subject matter are 9-16, 18-20 and 32-33 and such claims are herein acted on the merits.

Objection to the Specification

Applicant is requested to update the priority data found at line 1, page 1 of the present specification to properly reflect the status of each application to which the instant application claims priority. Applicant may wish to consider amending the priority information in the following manner:

---This application is a continuation of U.S. application no. 10/270,313 filed October 15, 2002, now U.S. Patent No. 6,777,444, which is a continuation of U.S. application no. 09/851,425 filed May 9, 2001, now U.S. Patent No. 6,608,108, which is a continuation-in-part of U.S. application no. 09/690,063, filed October 16, 2000, now U.S. Pat. No. 6,417,234, which is a continuation-in-part of U.S. application

no. 09/418,594, filed October 15, 1999, now U.S. Pat. No. 6,214,874, all of which are hereby incorporated by reference.---

Applicant's numerous amendments to the specification submitted in the Preliminary Amendment dated December 16, 2003 have been considered and reviewed. However, it is noted that the specification as originally filed was missing page 34, which contained the beginning portion of Example 14. Applicant has made no remarks regarding the fact that the amendments to the specification do not add new matter to the specification. However, since the present application is a direct continuation of U.S. Patent Application No. 10/270,313, which does contain page 34 and is identical to the subject matter that Applicant wishes to add to the specification by way of the Preliminary Amendment, Applicant is advised that an objection to the specification for adding new matter will not be made.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-12, 14-16, 18-20 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of papilloma, teratoma, adenoma or cervical carcinomas or leukemia (see present claim 13 and Example 9 of the present specification) by administering tetra-O-methylnordihydroguairaretic acid, does not reasonably provide enablement for the treatment of all tumor types by administering tetra-O-methylnordihydroguaiaretic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated

in the decision *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and,
8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The presently claimed invention is directed to a method for treating a tumor, comprising providing a composition comprising an effective amount of the compound tetra-O-methylnordihydroguaiaretic acid (i.e., M_4N) and applying the composition to the tumor, wherein the tumor may be malignant, benign, or a solid tumor, for example (see claims 11, 12 or 14).

In particular, one skilled in the art could not practice the presently claimed subject matter without undue experimentation because the artisan would not accept on its face that the treatment of any tumor type could be effectively achieved by the administration of the M_4N compound. Based upon the state of the art, as discussed below, the artisan would have only accepted that the treatment of specific tumor types could be achieved with this compound, M_4N, identified as having activity in treating such a tumor.

As set forth in *In re Marzocchi et al.*, 169 USPQ 367 (CCPA 1971):

"[A] [s]pecification disclosure which contains the teachings of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained*

therein which must be relied on for enabling support; assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling." (emphasis added)

The present claims circumscribe a method of treating any type of tumor by applying the M_4N compound. That is, in order to be enabled to practice the present invention, the skilled artisan would have to accept that by administering the presently claimed compound M_4N, all tumors, including papilloma, teratoma, adenoma, cervical cancer or leukemia, known in the art could be treated. In light of the fact that the specification not only fails to provide the skilled artisan with any direction or guidance as to how the treatment of any tumor type, aside from papilloma, teratoma, adenoma, cervical cancer or leukemia, could actually be achieved using the claimed M_4N compound, but also fails to direct the skilled artisan as to which other tumor types would be sensitive to this chemotherapeutic agent and how one would determine such sensitivity, and especially in light of the highly complex nature of tumors and cancer in general, the specification, which lacks an objective showing of which other tumors could be effectively treated using the claimed M_4N compound, is viewed as lacking an enabling disclosure of the entire scope of the claimed invention.

Here, the objective truth that any tumor type may be treated with the claimed M_4N compound is doubted because, while the state of the art of cancer treatment is well developed with regard to the treatment of specific cancer types with specific chemotherapeutic regimens (see Cecil's Textbook of Medicine, pages 1060-1074), the state of the art with regard to treating all tumors using a single agent is grossly underdeveloped.

In this regard, Cecil's Textbook of Medicine (2000) is cited. In particular, there is no known anticancer agent or combination of anticancer agents that is effective against treating all cancer types, nor is there any known anticancer agent or combination of agents that is effective against inhibiting the

growth of any type of cancer cell. The Cecil reference clearly shows that for the various known cancer types, there is not one specific chemotherapeutic agent or combination thereof that is effective at treating cancer or inhibiting the growth of cancer cells for each and every type of cancer (see Table 198-5 at page 1065; Tables 198-6 and 198-7 at pages 1066; Table 198-8 at page 1068; and Table 198-9 at page 1071).

Given that there was not known any specific agent or combination of agents effective to treat all known types of cancer, one of ordinary skill in the art would not accept on its fact Applicant's statement that such an objective could be achieved in any type of tumor using the presently claimed M_4N compound without enabling a set of species representative of the full scope of cancers known in the art. The artisan would have required sufficient direction as to how, at minimum, a representative set of species of cancer could be effectively treated with the M_4N compound and, further, how the artisan could have reasonably extrapolated such results to the larger and highly varied genus of tumors in general without requiring undue experimentation to determine what types of tumors would actually show sensitivity to the presently claimed M_4N compound, such that the artisan would have been imbued with at least a reasonable expectation of success in treating the tumor. Such success would not have been reasonable expected for all tumor types claimed given the highly complex and variable nature of all cancers known in the art and that Applicant has shown an example in cervical cancer cells and leukemia cells. To the artisan, the concept of a single agent effect to treat two specific tumor types would not have been considered representative or suggestive of the same efficacy in the treatment of all known types of tumor in the absence of any evidence or reasoning to do so. Additionally, since the skilled artisan would have expected the interaction of a particular agent in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for the use of each agent, one of skill in the art would have no other recourse but undue experimentation to undertake extensive testing to determine which other tumor types would be amenable to treatment using the claimed M_4N compound.

It is in this regard that Applicant is directed to the MPEP at §2164.08. All questions of enablement are evaluated against the claimed subject matter. Concerning the breadth of a claim relevant to enablement, the only relevant concern is whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of enablement involves the determination of how broad the claim is with respect to the disclosure and the determination of whether one skilled in the art is enabled to use the *entire scope* of the claimed invention without undue experimentation.

A conclusion of a lack of enablement must take into consideration the unpredictability in the art at the time of the invention and the direction or guidance provided by Applicant. The amount of guidance required to be present in the specification as originally filed is directly proportional to the amount of knowledge in the art as well as the unpredictability in the art. In other words, if little or nothing is known in the prior art about an aspect of the claimed invention and the art is unpredictable, the specification needs more detail and guidance as to how to use the invention in order to be enabling. Please reference *In re Fisher*, 417 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) and *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).

The enablement of the working examples provided in the specification is not disputed. However, they are not representative of the breadth of the presently claimed subject matter. Applicant's claims broadly claim the use of the M_4N compound for use in treating *any tumor*. The fact that Applicant has exemplified the use of this compound in cervical cancer cells or leukemia cells does not address the high degree of variability in the art in terms of the pathophysiological differences among tumor types and their reactivity to different anticancer compounds. Applicant has also failed to provide any evidence, or describe any protocol, that addresses this variability in the art such that one of ordinary skill in the art would have been imbued with at least a reasonable expectation of success in treating any tumor with the

claimed compound based on the direction provided in the present specification. While the lack of a working embodiment cannot be the sole factor in determining enablement, the absence of substantial evidence commensurate in scope with the presently claimed subject matter, in light of the unpredictable nature of the art and the direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

For example, the term "solid tumor" alone encompasses three distinctly different categories of tumors: (1) sarcomas, those that arise from connective or supporting tissues, such as bone or muscle; (2) carcinomas, those that arise from glandular tissues and epithelial cells; and (3) lymphomas, those that arise from the lymphoid organs, such as the lymph nodes, spleen or thymus. Though each of these three types can be lumped under the umbrella category of "solid tumor", the distinct etiology and pathophysiological differences between these three categories of solid tumor would not have imbued the skilled artisan with a reasonable expectation of success in treating any one or more of these types of solid tumor when efficacy had only been demonstrated in a single cervical cell line.

In light of such, it is clear that one of ordinary skill in the art would be faced with the impermissible burden of undue experimentation in order to execute the entire scope of the subject matter presently claimed. The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the pharmaceutical and chemical arts that experimentation in this particular art is not at all uncommon, but that the level of experimentation required in order to practice this aspect of the invention in the absence of any enabling direction by Applicant would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*." (emphasis added) Given the high degree of unpredictability noted and recognized in the art with regard to the treatment of tumors, the state of the art clearly precludes the general extrapolation of the results seen in two tumor types to the larger and much more highly varied

genus of tumors as a whole. In the absence of any direction or guidance presented by Applicant as to how such a therapeutic objective could be achieved without necessitating an undue level of experimentation, the present disclosure is viewed as lacking an enabling disclosure of the *entire scope* of the presently claimed subject matter.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of a medical doctor with several years of experience in the art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the use of the M_4N compound would have necessarily had efficacy in the treatment of any tumor type. In order to actually achieve such a result, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the presently claimed invention.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 32 is directed to "The method of claim 9, wherein the concentration of the compound is selected from the group consisting of: at least 20 μM, ..." and present claim 33 is directed to "The method of claim 9, wherein the concentration of the compound is selected from the group consisting of at least 10 μM...". There is insufficient antecedent basis for the limitation "the concentration of the compound" in both claim 32 and claim 33, since any reference to such a concentration in the claim from

which it depends (i.e., claim 9) is noticeably absent. It is unclear how Applicant intends present claims 32-33 to limit the presently claimed subject matter. As a result, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is properly rejected for rendering the scope of the claim indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-16 and 18-20 rejected under 35 U.S.C. 102(b) as being anticipated by Neiss et al. (U.S. Patent No. 5,276,060; 1994).

Neiss et al. teaches a method for the treatment of benign, premalignant and malignant solid tumors (col.2, lines 54-56), such as papilloma or adenoma (col.4, lines 6-11) or a variety of solid tumor (col.4, lines 3-17), comprising the application of pharmaceutical formulations containing a catecholic butane (col.2, line 54-col.3, line 5), such as the meso isomer of 1,4-bis(3,4-dimethoxy-phenyl)-2,3-dimethylbutane (col.6, lines 14-15), in combination with a pharmaceutically acceptable carrier (col.3, lines 29-31) and pharmaceutically acceptable adjuvant, such as the penetration enhancer dimethylsulfoxide (col.7, lines 48-62), wherein the catecholic butane may be applied directly to the situs of the abnormal growth of cells by topical application or by injection into the interior or near vicinity of the afflicted situs (col.3, lines 23-29). Neiss et al. discloses the treatment of mammals, including humans (col.3, lines 23-29 and 54-58).

Neiss et al. meets Applicant's limitation of "wherein said tumor is derived from transformed cells" in present claim 16 because the cancerous cells treated in the method disclosed by Neiss et al. are

necessarily "transformed" in the sense that they are no longer "normal" cells, but rather hyperproliferating and/or cancerous cells.

As previously stated *supra*, the elected compound tetra-O-methylnordihydroguaiaretic acid is also known as the meso isomer of 1,4-bis(3,4-dimethoxyphenyl)-(2R,3S)-dimethylbutane (please see Figure 1 of the instant drawings), which corresponds directly to the chemical compound of Neiss et al. Please also reference Neiss et al. at col.6, lines 11-15, where the reference further discloses all stereoisomeric configurations of the disclosed compound 1,4-bis(3,4-dimethoxyphenyl)-(2R,3S)-dimethylbutane, which anticipates the teaches the presently claimed limitation of the (2R,3S) configuration of the elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-16, 18-20 and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neiss et al. (U.S. Patent No. 5,276,060; 1994).

Neiss et al. teaches a method for the treatment of benign, premalignant and malignant solid tumors (col.2, lines 54-56), such as papilloma or adenoma (col.4, lines 6-11) or a variety of solid tumor (col.4, lines 3-17), comprising the application of pharmaceutical formulations containing a catecholic butane (col.2, line 54-col.3, line 5), such as the meso isomer of 1,4-bis(3,4-dimethoxy-phenyl)-2,3-dimethylbutane (col.6, lines 14-15), in combination with a pharmaceutically acceptable carrier (col.3, lines 29-31) and pharmaceutically acceptable adjuvant, such as the penetration enhancer dimethylsulfoxide (col.7, lines 48-62), wherein the catecholic butane may be applied directly to the situs of the abnormal growth of cells by topical application or by injection into the interior or near vicinity of the afflicted situs (col.3, lines 23-29). Neiss et al. discloses the treatment of mammals, including humans (col.3, lines 23-29 and 54-58).

As previously stated *supra*, the elected compound tetra-O-methylnordihydroguaiaretic acid is also known as the meso isomer of 1,4-bis(3,4-dimethoxyphenyl)-(2R,3S)-dimethylbutane (please see Figure 1 of the instant drawings), which corresponds directly to the chemical compound of Neiss et al. Please also reference Neiss et al. at col.6, lines 11-15, where the reference further discloses all stereoisomeric configurations of the disclosed compound 1,4-bis(3,4-dimethoxyphenyl)-(2R,3S)-dimethylbutane, which clearly teaches the presently claimed limitation of the (2R,3S) configuration of the elected species.

The differences between the Neiss et al. reference and the presently claimed subject matter lies in that the reference fails to teach the particular concentrations of tetra-O-methylnordihydroguaiaretic acid as recited in present claims 32-33.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because the determination of the optimum concentrations of the presently claimed active agent that comprises the composition would have been a matter well within the purview of one of ordinary skill in the art. Such a determination

would have been made in accordance with a variety of factors, such as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the concentrations that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific concentrations are not seen to be inconsistent with those that would have been determined by the skilled artisan.

In addition, the concentration of the active ingredient is a result-effective variable, i.e., a variable that achieves a recognized result, and, therefore, the determination of the optimum of workable dosage range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s).

Double Patenting

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9-10, 14-16, 18-20 and 32-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over patented claims 1-8 U.S. Patent No. 6,214,874.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s).

Although the conflicting claims are not identical, the patented claims render the present claims obvious.

The patented claims clearly provide for the treatment of a tumor (i.e., an HPV-induced tumor) by applying the compound tetra-O-methylnordihydroguaiaretic acid to said tumor in an effective amount, wherein the tumor is cervical or oral cancer or is derived from transformed cells, such as C3 cells, and the tetra-O-methylnordihydroguaiaretic acid compound is administered with at least one pharmaceutically acceptable excipient or carrier, such as dimethylsulfoxide. Though the present claims are directed to the treatment of a tumor in general (see present claim 9), claims directed to a species will always anticipate a genus. Please reference MPEP §2131.02 for a discussion of genus-species situations and also *In re Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960) and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). Though the patented claims are silent as to the concentration of the active agent, the determination of the optimum concentrations to be applied to the tumor would be well within the routine skill of the artisan and are not seen to differ significantly from those that would have been determined from the patented claims.

Accordingly, claims 9-10, 14-16, 18-20 and 32-33 are properly rejected as claiming obvious and unpatentable variants of patented claims 1-8 of U.S. Patent No. 6,214,874.

Claims 9-15, 18, 20 and 32-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over patented claims 1-9 U.S. Patent No. 6,417,234.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s).

Although the conflicting claims are not identical, the patented claims render the present claims obvious.

The patented claims clearly provide for the treatment of a tumor by applying the compound tetra-O-methylnordihydroguaiaretic acid to said tumor in an effective amount, wherein the tumor is malignant (i.e., squamous cell, adenocarcinoma or medulloblastoma) or benign (i.e., papilloma, teratoma or adenoma) or is a solid tumor and where the tetra-O-methylnordihydroguaiaretic acid compound is administered with at least one pharmaceutically acceptable excipient or carrier. Though the patented claims are silent as to the concentration of the active agent, the determination of the optimum concentrations to be applied to the tumor would be well within the routine skill of the artisan and are not seen to differ significantly from those that would have been determined from the patented claims.

Accordingly, claims 9-15, 18, 20 and 32-33 are properly rejected as claiming obvious and unpatentable variants of patented claims 1-9 of U.S. Patent No. 6,417,234.

Claims 9-12, 14-15, 18-20 and 32-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over patented claims 9, 11-14, 17-27 and 41-42 of U.S. Patent No. 6,608,108.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are

not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s).

Although the conflicting claims are not identical, the patented claims render the present claims obvious.

The patented claims clearly provide for the treatment of a tumor (i.e., cancerous or non-cancerous types, as well as cervical, oral, penile or head and neck, which are solid tumors) by injecting the compound tetra-O-methylnordihydroguaiaretic acid into said tumor in an effective amount, wherein the tetra-O-methylnordihydroguaiaretic acid compound is administered with at least one pharmaceutically acceptable excipient or carrier, such as dimethylsulfoxide. Though the patented claims are silent as to the concentration of the active agent, the determination of the optimum concentrations to be applied to the tumor would be well within the routine skill of the artisan and are not seen to differ significantly from those that would have been determined from the patented claims.

Additionally, although patented claim 42 is directed to systemic delivery of the tetra-O-methyldihydroguaiaretic acid, the determination of the optimum route of administration of the active agent would have also been well within the routine skill of the artisan who was well apprised of methods of adapting pharmaceutical agents for use in various modes of delivery. Furthermore, one of skill in the art would have been motivated to alter the route of administration to exert better control over the time to therapeutic activity or, for example, to avoid toxicity associated with rapid onset routes of administration, i.e., intravenous, sublingual, etc.

Accordingly, claims 9-12, 14-15, 18-20 and 32-33 are properly rejected as claiming obvious and unpatentable variants of patented claims 1-8 of U.S. Patent No. 6,608,108.

Conclusion

Rejection of claims 9-16, 18-20 and 32-33 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Leslie A. Royds
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Art Unit 1614

November 6, 2006

11/12/06
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SUPERVISORY PATENT EXAMINER